CLAIMS

1. A method of activating serum and glucocorticoid-induced protein kinase (SGK) wherein the SGK is phosphorylated.

2. A method of reducing the activity of phosphorylated SGK wherein the SGK is dephosphorylated.

3. The method of claim 1 wherein the SGK is phosphorylated by PDK1 or a variant, fragment, fusion or derivative thereof, or a fusion of a said variant, fragment or derivative.

4. The method of claim 2 wherein the SGK is dephosphorylated by PP1 or PP2C or PP2A or a variant, fragment, fusion or derivative thereof, or a fusion of a said variant, fragment or derivative.

5. Use of PP1 or PP2C or PP2A or a variant, fragment, fusion or derivative thereof, or a fusion of a said variant, fragment or derivative in a method of deactivating and/or dephosphorylating SGK.

6. Use of PDK1 or a variant, fragment, fusion or derivative thereof, or a fusion of a said variant, fragment or derivative in a method of activating and/or phosphorylating SGK.

7. A method of activating SGK wherein SGK is phosphorylated on the residue equivalent to Thr256 of full-length human SGK1.

8. A method of activating SGK wherein SGK is phosphorylated on the residue equivalent to Ser422 of full-length human SGK1.

9. A method according to claim 8 wherein SGK is further phosphorylated on the residue equivalent to Thr256 of full-length human SGK1.

10. A method according to claim 1 wherein SGK is activated and/or phosphorylated by a preparation containing PDK2 activity.

11. A fusion polypeptide that comprises human SGK or a variant, fragment or derivative thereof.

12. A fusion polypeptide according to claim 11 wherein the fusion polypeptide comprises glutathione-S-transferase.

13. A fusion polypeptide according to claim 11 or 12 or wherein the fusion polypeptide comprises a fragment of human SGK or variant or derivative thereof wherein residues equivalent to the N-terminal about 20, 30, 40, 50 or 60 amino acids of human full-length SGK1 are not present.

14. A polypeptide comprising the amino acid sequence of human SGK or a fragment, variant, derivative or fusion thereof wherein the residue equivalent to serine 422 of full-length human SGK1 is replaced and/or the residue equivalent to threonine 256 of full-length human SGK1 is replaced and/or the residue equivalent to lysine 127 of full-length human SGK1 is replaced.

15. A polypeptide according to claim 14 wherein the residue equivalent to serine 422 of full-length human SGK1 is replaced by an aspartate, glutamate, alanine or other non-phosphorylatable residue and/or the

residue equivalent to threonine 256 of full-length human SGK1 is replaced by an alanine or other non-phosphorylatable residue and/or the residue equivalent to lysine 127 of full-length human SGK1 is replaced by an alanine residue.

16. A polypeptide according to claim 15 wherein the residue equivalent to serine 422 of full-length human SGK1 is replaced by an aspartate residue and the residues equivalent to threonine 256 and lysine 127 of the full-length human SGK1 remain as threonine and lysine respectively.

17. A polypeptide according to claim 16 wherein residues equivalent to the N-terminal 20, 30, 40, 50 or 60 amino acids of full-length human SGK1 are not present.

18. A polynucleotide encoding a polypeptide as defined in any one of claims 11 to 17 .

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19. A recombinant polynucleotide suitable for expressing a polypeptide as defined in any one of claims 11 to 17.

20. A host cell comprising a polynucleotide or as defined in claim 18 or 19.

21. A method of making the polypeptide as defined in any one of claims 11 to 17 the method comprising culturing a host cell comprising a recombinant polynucleotide or a replicable vector which encodes said polypeptide, and isolating said polypeptide from said host cell.

22. A method according to claim 21 further comprising treating the host cell such that the polypeptide is activated and/or phosphorylated.

23. A method according to claim 22 wherein the host cell is treated by exposing it to IGF-1 and/or hydrogen peroxide.

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24. A polypeptide obtainable by the method of any one of claims 21 to 23.

25. A method of identifying a compound that modulates the activity of SGK wherein activated SGK is used.

26. A method of identifying a compound that modulates the activity of SGK, the method comprising contacting a compound with SGK and determining whether the activity of the said SGK is changed compared to the activity of the said SGK in the absence of said compound wherein the activity of SGK is measured by measuring the phosphorylation by SGK, in the presence of a suitable phosphate donor, of a polypeptide comprising an amino acid sequence corresponding to the consensus sequence (Arg/Lys; preferably Arg)-X-(X/Arg)-X-X-(Ser/Thr)-Z, wherein X indicates any amino acid, X/Arg indicates any amino acid, with a preference for arginine, and Z indicates that the amino acid residue is preferably a hydrophobic residue.

27. The method of claim 25 or claim 26 wherein the said SGK or activated SGK is a SGK wherein the residue equivalent to serine 422 of full-length human SGK1 is replaced by an aspartate residue and the residues equivalent to threonine 256 and lysine 127 of the full-length human SGK1 remain as threonine and lysine respectively.

28. The method of any one of claims 25 to 27 wherein the SGK is SGK activated by phosphorylation.

29. The method of any one of claims 24 to 28 wherein the activity of the SGK is decreased in the presence of the compound.

30. The method according to claim 25 or 26 wherein the activity of the SGK is increased in the presence of the compound.

31. A method of identifying a compound which binds to a physiological substrate of SGK, such as BAD or GSK3, and either enhances or prevents its activation and/or phosphorylation by SGK, the method comprising determining whether a compound enhances or prevents the interaction of the said substrate with SGK or determining whether the compound substantially blocks phosphorylation and/or activation of said substrate by SGK.

32. A method of identifying a compound which modulates the activation of SGK by an interacting polypeptide, such as PDK1 or a polypeptide with PDK2 activity, the method comprising determining whether a compound enhances or disrupts the interaction between (a) SGK and (b) the interacting polypeptide, such as PDK1 or a functional equivalent of PDK1 or a preparation containing PDK2 activity, or determining whether the compound modulates activation of the said SGK by the interacting polypeptide, such as PDK1 or a preparation containing PDK2 activity or a functional equivalent thereof.

33. A method of identifying a polypeptide that interacts with activated SGK, the method comprising (1) contacting (a) the said SGK with (b) a composition that may contain a polypeptide that interacts with the said activated SGK, (2) detecting the presence of a complex containing the said SGK and a polypeptide, and optionally (3) identifying any polypeptide bound to the said protein kinase.

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34. A kit of parts useful in carrying out a method according to any one of claims 25 to 33.

35. A kit of parts according to claim 34 comprising SGK, PDK1 or a functional equivalent thereof, a preparation containing PDK2 activity or a functional equivalent thereof and/or a substrate of SGK, for example Crosstide or BAD or GSK3.

36. Use of a compound that inhibits SGK but does not inhibit PKB in a method of identifying a substrate of SGK.

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37. A compound identifiable or identified by a method according to any one of claims 25 to 33.

38. A compound according to claim 37 for use in medicine.

39. Use of a compound according to claim 37 in the manufacture of a medicament for treatment of a patient in need of modulation of the activity of SGK.

40. A method of treating a patient in need of modulation of the activity of SGK wherein the patient is administered a effective amount of a compound according to claim 37.

41. Use of activated SGK in a screening assay for a drug-like compound or lead compound for the development of a drug-like compound.

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42. The use according to claim 39 or method according to claim 40 wherein the patient has cancer.

43. The use according to claim 39 or method according to claim 40 wherein the patient has diabetes or ischaemic disease.

44. The method, use, fusion polypeptide, polypeptide or kit of parts according to any one of claims 1 to 17, 25 to 33, 35, 39 to 43 wherein the said SGK is SGK1, SGK2α, SGK2β or SGK3.

Add A8